**Cover letter for Nature Genetics**

Although optional, the cover letter is an excellent opportunity to briefly discuss the context and importance of the submitted work and why it is appropriate for the journal. Please avoid repeating information that is already present in the abstract and introduction. The cover letter is not shared with the referees, and should be used to provide confidential information, such as conflicts of interest, and to declare any related work that is in press or submitted elsewhere.

Research into the genetic basis of the plant immune response has given us a clear picture of how interactions between plant hosts and specialist pathogens cause simple disease outcomes. For example, when a specialist pathogen attacks a host plant, disease or defense can be determined by interactions between a single plant gene and a single corresponding pathogen gene. Thus, variation within a small number of genes causes large, binary changes to the disease phenotype. Many of these genes are well characterized through molecular and functional studies in plant pathology.

We understand less clearly how complex genetics in the host and pathogen control disease phenotypes with continuous variation. These quantitative interactions are common between generalist pathogens and their varied plant targets. Such generalist pathogens may attack multiple species and genera of plants, and even individual genotypes within the pathogen species can generalize. Disease phenotype variation can respond to small effects of genetic variation at many loci in both the host and in the generalist pathogen. It remains to be seen which genes in the host and pathogen control this phenotypic variation. In this paper, we conducted a genomic analysis to identify thousands of loci with small effects contributing to lesion size in quantitative plant-pathogen interactions.

Plants have undergone artificial selection by humans for thousands of years, leading to their domestication as cultivated crop species. Domestication often drastically reduces the genetic variation of a plant species, as only a small subset of the wild ancestors are cultivated and bred. This can in turn reduce genetic variation available to control plant defenses against pathogens, and may increase the vulnerability of the domesticated plants to disease. Even so, the effect of domestication on the genetics of pathogen resistance is largely unstudied. Here, we examine how domesticated tomato immunity to a collection of pathogen genotypes differs from immunity in tomato’s closest wild relative. We aim to understand how evolution under domestication has altered interactions genome-wide between pathogen and host.

To delve into the genetics of pathogen virulence and the effects of plant domestication, we focused on genetically distinct individuals of the common fungal pathogen, *Botrytis cinerea*. *Botrytis* is an extreme generalist, with the ability to form lesions and cause disease on nearly all flowering plant species (eudicots). *Botrytis* is a major pathogen threat to many domesticated crop plants, including wine grapes and tomato. To examine the effect of domestication on tomato susceptibility to *Botrytis*, we compared geographically distinct wild tomato genotypes to domesticated tomato genotypes with distinct fruit traits.

We feel that this work is well suited to the interests of Nature Genetics. In this paper we focus on genome-wide variation associated with a complex disease that is common across a multitude of plants, including many species of agricultural importance. We also ask how domestication has shaped the evolution of plant defenses and the virulence of their pathogens. This research has implications for…